(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for ceftizoxime content, sterility, pyrogens, moisture, pH, identity, and crystallinity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(*a*) If the batch is packaged for repacking or for use in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing at least 500 milligrams.

(*2*) For sterility testing: 20 packages, each containing equal portions of approximately 300 milligrams.

(*b*) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 10 immediate containers; or if each container contains less than 1 gram of ceftizoxime, a minimum of 20 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Ceftizoxime content.* Proceed as directed in §436.345 of this chapter.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(b) of this chapter, using a solution containing 50 milligrams of ceftizoxime per milliliter.

(4) *Moisture.* Proceed as directed in §436.201 of this chapter.

(5) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(6) *Identity.* From the high-pressure liquid chromatograms of the sample and the ceftizoxime working standard determined as directed in paragraph (b)(1) of this section, calculate the adjusted retention times of the ceftizoxime in the sample and standard solutions as follows:

$$\text{Adjusted retention time of ceftizoxime} = t - t_a$$

where:

t = Retention time measured from point of injection into the chromatograph until the maximum of the ceftizoxime sample or working standard peak appears on the chromatogram; and

t_a = Retention time measured from point of injection into the chromatograph until the maximum of nonretarded solute appears in the chromatogram.

The sample and the ceftizoxime working standard should have corresponding adjusted ceftizoxime retention times.

(7) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[48 FR 46271, Oct. 12, 1983; 48 FR 49656, Oct. 27, 1983, as amended at 55 FR 11583, Mar. 29, 1990]

§442.18 Cefuroxime sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefuroxime sodium is the sodium salt of (6*R*,7*R*)-3-carbamoyloxymethyl-7-[(2*Z*)-2-(2-furyl)-2-methoxyiminoacetamido]cepha-3-em-4-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 855 micrograms and not more than 1,000 micrograms of cefuroxime activity per milligram on an anhydrous basis.

(ii) Its moisture content is not more than 3.5 percent.

(iii) The pH of an aqueous solution containing 100 milligrams of cefuroxime per milliliter is not less than 6.0 and not more than 8.5.

(iv) It gives a positive identity test for cefuroxime.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research: 10 packages, each containing approximately 1 gram.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in §442.343.

(2) *Moisture.* Proceed as directed in §436.18a(b)(4) of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams of cefuroxime per milliliter.

(4) *Identity.* Proceed as directed in § 442.18a(b)(6).

[54 FR 40654, Oct. 3, 1989; 54 FR 50686, Dec. 8, 1989]

§ 442.18a Sterile cefuroxime sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefuroxime sodium is the sodium salt of (6*R*, 7*R*)-3-carbamoyloxy-methyl-7-[(2*Z*)-2-(2-furyl)-2-methoxyiminoacetamido] cepha-3-em-4-carboxylic acid. It is so purified and dried that:

(i) If the cefuroxime is not packaged for dispensing, its cefuroxime content is not less than 855 micrograms and not more than 1,000 micrograms of cefuroxime per milligram on an anhydrous basis. If the cefuroxime is packaged for dispensing, its cefuroxime content is not less than 855 micrograms and not more than 1,000 micrograms of cefuroxime per milligram on an anhydrous basis and also, each container contains not less than 90 percent and not more than 120 percent of the number of milligrams of cefuroxime that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) Its moisture content is not more than 3.5 percent.

(v) Its pH in an aqueous solution is not less than 6.0 and not more than 8.5.

(vi) It gives a positive identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for cefuroxime content, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(*a*) If the batch is packaged for repacking or for use as an ingredient in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 1 gram.

(*2*) For sterility testing: 20 packages, each containing approximately 1 gram.

(*b*) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefuroxime content.* Proceed as directed in § 436.343 of this chapter.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 50 milligrams of cefuroxime per milliliter.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter, using the titration procedure described in paragraph (e)(1) of that section.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(6) *Identity.* From the high-pressure liquid chromatograms of the sample and the cefuroxime working standard determined as directed in paragraph (b)(1) of this section, calculate the adjusted retention times of the cefuroxime in the sample and standard solutions as follows:

$$\text{Adjusted retention time of cefuroxime} = t - t_a$$

where:

t = Retention time measured from point of injection into the chromatograph until the maximum of the cefuroxime sample or working standard peak appears on the chromatogram; and

t_a = Retention time measured from point of injection into the chromatograph until the maximum of nonretarded solute appears in the chromatogram.

The sample and the cefuroxime working standard should have corresponding adjusted cefuroxime retention times.

[48 FR 38461, Aug. 24, 1983, as amended at 55 FR 11583, Mar. 29, 1990]

§ 442.19 Cefuroxime axetil.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefuroxime axetil is an amorphous mixture of the diastereoisomers of 5-thia-1-azabicyclo[4.2.0]oct-